# Lecture 1 – 08/29/12 **ORIENTATION TO PHARMACOLOGY; FEDERAL DRUG LAWS**

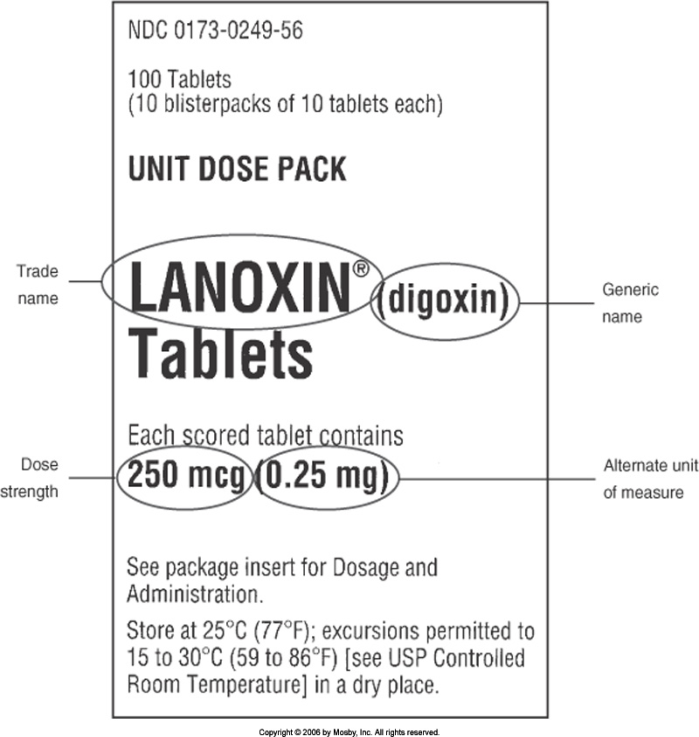
**(Adams Ch. 1 & 2)**

* **Objectives**
  + Know role of drug knowledge in nursing practice
  + Know role of FDA
  + Evaluate sources of drug info

## CH. 1 – Intro to Pharmacology: Drug Regulation and Approval

* **Root Derivation** **(Greek**) (1.2)
  + *Pharmakon* = medicine
  + *Logos* = study
* **History of Pharmacology** (1.1)
  + Roots in herbal medicine
    - One of the oldest forms of healthcare
    - Humans using plants to relieve symptoms of dz
    - Has been used in virtually every culture throughout Hx
  + 3000 BC – Babylonians - earliest recorded prescriptions written on clay tablets
  + ~2700 BC – Chinese wrote *Pen Tsao* (Great Herbal) – a compendium of plant remedies
  + 1500 BC – Egyptians wrote *Eber’s Papyrus* – documentation of remedies
  + 1693 (AD) – First reference to the word “pharmacology” in a text by Samuel Dale
* **Modern Pharmacology** (1.1)
  + Thought to have begun in the early 1800s
    - Chemists became able to isolate specific substances from complex natural products
    - Allowed for the study of effects based on standardized doses
      * Early pharmacologic agents
        + morphine (first isolated in 1805 by Serturner)
        + colchicines
        + curare
        + cocaine
  + 1847 – First Department of Pharmacology – Estonia
  + 1890 – First US Department of Pharmacology – University of Michigan
    - John Jacob Abel, its founder, considered father of American pharm
  + 1900s
    - Exponential increase in pace of change in all areas of medicine
    - Isolation of drug active ingredients could now be accomplished in a lab
      * Based on new knowledge of molecular structures
      * This ↑ the pace and volume of drug **synthesis**
    - It became possible to understand HOW drugs produce their effects
      * Again, based on molecular studies
      * Scientists able to discover **drugs’ molecular mechanism of action**
        + **The most important aspect of pharmacology**
  + Current Practice
    - Comparatively very complex and advanced, but important to remember roots
* **Major purpose of pharmacology** (1.1)
  + **To improve quality of life and relieve human suffering**
* **The Study of Pharmacology** (1.2)
  + **Encompasses:**
  1. How drugs are administered
     + PO/IV/IM/SQ/anal/transdermal/etc 🡪 to the blood stream
  2. Where they travel in the body
     + Through the blood to target cells
  3. Responses they produce
     + Therapeutic applications
       - i.e.: Abx 🡪 ↓ bacteria
     + Side-effects
     + Interactions
  + Over 10,000 drugs are currently available, each with unique sets of these 3 factors
    - Proper administration 🡪 dramatic improvement of quality of life is possible
    - **Improper administration 🡪 devastating consequences (possible toxicity, or ineffectiveness)**
    - Many drugs produce multiple responses, and are prescribed for more than 1 dz
      * Different responses elicited by individual patient factors (age, sex, BMI, health status, genetics, etc.)
  + An important consideration is a drug’s **bioavailability**
    - i.e.: 50%, 80%...
    - Affected by route of administration, individual metabolism, brand name vs. generic, etc.
    - This is an important consideration because some drugs can cause negative effects, such as toxicity, at high doses. Therefore, dose level is very important, and requires a lot of research.
* **Pharmacology & Therapeutics** (1.3)
  + Pharm is at the core of patient care and is integrated into every step of the nursing process
  + Nurse’s Responsibility
    - Manage, monitor, evaluate, and educate patients about proper medication usage
    - **Nurse has primary responsibility for observing the effects of drugs administered to patients**
      * Therefore, know monitoring protocol (q15m, q30m) to check on patient to observe for adverse reactions
        + Especially important when administering a drug a patient has never taken before
* **Nurse Needs to Know:**
  + **Generic and Trade Name of drugs**
    - MEMORIZE GENERIC (and trade) NAMES
      * Trade names can be changed (patent period = 17y)
      * One generic can have 10+ trade names
  + **Usual dosage**
  + **Route of administration**
  + **Indication**
  + **Action**
  + **Adverse reaction**
  + **Nursing Implications**

BEFORE EACH CLINICAL, LOOK UP YOUR PATIENT’S DRUGS  
AND KNOW ALL THESE CATEGORIES

* **Classification of Therapeutic Agents** (1.4)
  + Therapeutics = branch of medicine that deals with prevention of dz and treatment of suffering
    - 3 Classes:
      * Medications (drugs)
      * Biologics
      * Alternative Therapies
  + Drugs
    - Chemical agents capable of producing biologic responses within the body
    - After administration 🡪 drugs are called medication
    - i.e.: Advil, Tylenol, abx
  + Biologics
    - Agents naturally produced in animal cells
    - i.e.: Ab, hormones, blood products enteral bacteria (🡪K-vit), interferons, vaccines
  + Alternative Therapies
    - Natural plant extracts/herbs/vitamins/minerals/dietary supplements
    - Therapeutic techniques considered by some to be unconventional
    - i.e.: acupuncture, hypnosis, biofeedback, massage, herbals, vitamins
* **Pharmacotherapeutics**
  + Pharmacotherapy: the application of drugs to prevent dz and ease suffering
  + Why do we use medications?
    - Acute – requires immediate response
      * i.e.: ↓ pain
    - Maintenance – control of chronic dz
      * i.e.: diabetes, BP regulation
    - Supplemental – repair deficiency
      * i.e.: vitamins/minerals (Fe, Ca)
* **Prescription vs. OTC** (1.5)
  + Prescription
    - Requires MD/NP order
    - ADVANTAGE: exam required, leading to a specific diagnosis, resulting in proper drug and dose
    - DISADVANTAGE: cost
  + OTC
    - Does not require MD/NP order
    - ADVANTAGE: less time and money
    - DISADVANTAGE: lack of exam, meaning a HCP’s diagnosis cannot be made, which may lead to a person using the wrong drug at the wrong dose. No patient education. This can cause progression of unrecognized dz
* **Drug Regulations and Standards** (1.6)
  + Few standards/guidelines to protect the public until the 1800s
    - Many concoctions were ineffective; some contained dangerous or addictive substances
  + First standard was a list of drugs and drug recipes called a **formulary**
  + **1820** **- US Pharmacopoeia (USP)** made
    - First standard compendium
    - Comprehensive publication of drug standards
    - Provides standards of drug purity, and directions for synthesis
    - USP label on many current medications
  + 1852 – APhA was founded
    - Professional society of pharmacists
    - Established the National Formulary (NF)
  + 1852-1975 – USP and NF worked together as separate publications
    - USP – covered all drug products
    - NF – covered pharmaceutical ingredients
  + 1862 – Federal Bureau of Chemistry established
    - under president Lincoln
    - This evolved into the FDA (1988)
  + 1902 – Biologics Control Act
    - Helped standardize the quality of blood-related products
  + 1906 – Pure Food and Drug Act
    - Gave the government power to control medication labeling
  + 1912 – Sherley Amendment
    - Prohibited the sale of drugs labeled with fraudulent therapeutic claims
  + **1938** **– Food, Drug, and Cosmetic Act**
    - First law preventing the sale of drugs that had not been thoroughly tested before marketing
    - Later amendments required drug companies to prove the safety and efficacy of any drug before it could be sold in the US
  + 1944 – Public Health Service Act passed by congress
    - Covered many health issues, including:
      * Biological products
      * Control of communicable dz
  + 1975 – USP and NF merged into one publication 🡪 USP-NF
    - The current document: ~4,000 drug monographs
    - Printed q5y
  + 1986 – Childhood Vaccine Act
    - Authorized FDA to:
      * acquire information about patients receiving vaccines
      * recall biologics
      * recommend civil penalties if guidelines regarding biologics were not followed
  + **1988 – FDA** founded
    - Agency of the US Department of Health and Human Services
    - Ensures the safety and effectiveness of drugs
    - Any pharmaceutical lab MUST obtain FDA approval before marketing a drug (details – 1.7)
  + 1992 – Prescription Drug User Fee Act
    - Requires manufacturers of nongeneric drugs & biologics to pay fees used for improvements in the drug review process.
  + **1994 – Dietary Supplement Health and Education Act**
    - Requires clear labeling of dietary supplements (i.e.: vitamins)
    - Gives the FDA the power to take harmful substances off the market
  + 1997 – FDA Modernization Act
    - Reauthorized Prescription Drug User Fee Act of 1992
    - Largest reform effort of the drug review process since 1938 (Food, Drug, & Cosmetic Act)
  + 2002 – Bioterrorism Act
    - Implemented guidelines for registration of selected toxins that could pose a public health threat (including animal and plant safety)
  + 2007 – FDA Amendments Act
    - Allowed additional comprehensive reviews of new drugs and medical products
    - Extends the FDA Modernization Act of 1997
    - Includes FDA Critical Path Initiative
      * Effort to modernize the sciences to enhance the use of bioinformation to improve the “safety, effectiveness, and manufacturability of candidate medical products.”
* Role of FDA (1.7)
  + Center for Drug Evaluation and Research (CDER)
    - Controls whether drugs (Rx & OTC) can be used for therapy
  + Center for Biologics Evaluation and Research (CBER)
    - Regulates the use of biologics
  + Center for Food Safety and Applied Nutrition (CFSAN)
    - Oversees administration of herbal products and dietary supplements
* **Stages of Approval for Therapeutic and Biologic Drugs** (1.8)
  + Stages of Approval for New Drugs
    - Preclinical
      * Extensive laboratory research – animals or human cells
      * Looks at effect of different doses and for adverse effects
      * Predict whether or not a drug will cause harm to humans
    - Clinical
      * Longest phase
      * 3 clinical phase trials
        + Clinical Phase I-III
      * First, clinical pharmacologists perform tests on healthy volunteers to determine dose and adverse effects
      * Then, large group of patients with dz are given the medication
      * Evaluation by medical specialists (clinical investigators) to address concerns
      * In special cases, drug may sometimes be used immediately with careful monitoring if all goes well in clinical phase trials
    - NDA (New Drug Application) Review
      * Review of all new drugs by FDA
        + FDA is allowed 6 months to initially review an NDA – avg total review time = 17-24m
        + If NDA is rejected, process is suspended until noted concerns are addressed
      * IND – Investigational New Drug Application
        + May be submitted for Phase I clinical trials when a stellar new drug is evaluated
    - Post Marketing Surveillance
      * Purpose: to survey for harmful drug effects in a larger population
        + Because some adverse effects take longer to appear
      * FDA hold public meetings annually to receive feedback
      * FDA has recalled 11 prescription drugs between 1997 and 2000.
        + i.e.: troglitazone (Rezulin) was recalled in 2000 after HC providers asked the FDA to reconsider its benefits vs. its risks (it was linked to death, liver failure, and heart failure)
* Recent Changes to Drug Approval Process (1.9)
  + In the 1990s, government officials began to consider how they could speed up the review process (in response to pressure from organized consumer groups and various drug manufacturers)
  + This led to the Prescription Drug User Fee Act of 1992
    - Requires drug and biologic manufacturers to provide yearly product user fees
    - 🡪 Additional income for the FDA 🡪 more employees, more money, more efficiency!
  + In 1997, the FDA Modernization Act re-approved the Prescription Drug User Fee Act
    - Even more money and efficiency…
  + In 2007, the FDA Amendments Act expanded the reform…
    - Allowing more US resources to be used for comprehensive review of new drugs
* Canadian Drug Standards (1.10)
  + We don’t have to know these
* Nurses and the Drug Approval Process (1.11)
  + Most frequent opportunity to participate in Phase IV (postmarketing surveillance)
  + Monitor therapeutic and adverse effects
  + Report drug reactions and adverse effects

## CH. 2 – Drug Classes and Schedules

* **Therapeutic and Pharmacologic Classification of Drugs** (2.1)
  + 2 classes widely used:
    - Pharmacological Class
      * HOW a drug produces its effect
        + Molecular, tissue, and body system level
        + Eg: Antihypertensives:

Lower plasma volume 🡪 diuretic

Blocks hormonal activity 🡪 ACE inhibitor

Blocks physiologic rxns to stress 🡪 adrenergic antagonist

* + - Therapeutic Class
      * WHAT a drug does clinically
        + Usefulness in treating a particular dz

Lower blood cholesterol 🡪 antihyperlipidemics

Restore N cardiac rhythm 🡪 antidisrhythmics

Treat angina 🡪 antianginals

* + Other (less common) classes:
    - Chemical Class
      * i.e.: fluoroquinolones, cephalosporins, thiazides
      * Knowing these will become invaluable in understanding adverse rxns
    - Prototype Drug
      * Individual drugs that represent their entire group (usually the 1st to be developed)
        + i.e.: Morphine is the prototype of opioid analgesics
  + Example of classifications
    - Morphine:
      * Pharmacologic – opioid agonists / CNS Depressants
      * Therapeutic – opioid analgesics
      * Chemical – opiate
* **Chemical, Generic, and Trade Names for Drugs** (2.2)
  + Drug Names
    - Chemical
      * Only 1 name (IUPAC name)
        + Useful chemical names: lithium carbonate, calcium gluconate, sodium chloride
        + Useful in understanding physical and chemical properties
      * Complicited and difficult to remember
        + i.e.: Diazepam = 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one
    - Generic
      * Only 1 name
      * Assigned by US Adopted Name Council
      * Written in **lower case**
      * Many organizations (i.e.: FDA, WHO) describe meds by their generic names
      * **MEMORIZE THESE**
    - Trade
      * May have several names (because patent expires after 17y)
      * Assigned by the company marketing the drug
      * **CAPITALIZED**
  + After 17y, competing companies may sell generic equivalents of trade name drugs, sometimes by using a different name which must be approved by the FDA
    - 17y gives original pharmaceutical company time to recover from the expenses incurred developing the drug
    - However, time spent in approval is usually subtracted from the 17y…
  + Combination drug
    - Contains more than 1 active generic ingredient
* **Differences Between Brand-Name Drugs and Their Generic Equivalents** (2.3)
  + Bioavailability
    - The physiologic ability of a drug to reach its target cells and produce its effect
    - Can be effected by inert ingredients and tablet compression
    - Measured by how long a drug takes to exert its effects
    - Criticality is relative to what the drug’s use is
    - Negative Formulary Lists
      * Lists of trade-name drugs that cannot be dispensed as generics
      * Controversial – difference in bioavailability and bioequivalence may sometimes affect patient outcomes; however, consumer advocacy groups are concerned with higher cost of trade-name drugs.
  + Price
    - Exclusive rights to produce a drug 🡪 no competition 🡪 prices generally quite high
* **Controlled Substances and Drug Schedules** (2.4)
  + Addiction: overwhelming feeling that drives a person to repeatedly use a drug
  + Dependence: a physiologic or psychologic need for a substance
    - Physical dependence: condition caused by adaptation of the nervous system to repeated drug use
      * Drug use cessation causes withdrawal
    - Psychological dependence: no physical withdrawal upon cessation, but intense compelling desire to continue drug use
  + 1970 – Controlled Substances Act (AKA Comprehensive Drug Abuse Prevention and Control Act)
    - Drugs that cause dependency are restricted to situations of medical necessity, if allowed at all
  + 5 Schedules
    - Schedule I – no therapeutic use and high potential for abuse
      * i.e.: heroin, LSD, marijuana, methaqualone (Quaalude)
    - Schedule V – least potential for abuse; used OTC
      * i.e.: OTC cough medicines with codeine, diphenoxylate with atropine (subtherapeutic qty of atropine added to discourage deliberate overdose of diphenoxylate)
  + Not all drugs with abuse potential are regulated or put into schedules (caffeine, alcohol, tobacco)
  + Hospitals and pharmacies using controlled substances must register with FDA and DEA, and are assigned a registration number to purchase scheduled drugs
    - Complete records of all quantities bought and sold must be maintained
  + Those who prescribe scheduled drugs must also register with the DEA and receive an assigned #
  + One nurse alone cannot dispose of controlled substances – 2 people are necessary to sign off
* Canadian Regulations Restricting Drugs of Abuse (2.5)
  + We don’t have to know these
* **Where do Nurses get Medication Information???**
  + Drug Handbooks
  + Micro-Medex (online)
  + **Pharmacists**
    - Our biggest ally – should be consulted whenever we are unable to find the info we need
* **PRACTICE**
  + Rocephin
    - Generic name: ceftriaxone
    - Trade names: Rocephin
    - Therapeutic class: anti-infective
    - Pharmacologic class: 3rd generation cephalosporin
    - Schedule: not scheduled
  + Hydrocodone
    - Generic name: hydrocodone
    - Trade names: Tussigon
    - Therapeutic class: narcotic analgesic, antitussive
    - Pharmacologic class: opioid; narcotic agonist
    - Schedule: III
  + Nexium
    - Generic name: esomeprazole
    - Trade names: Nexium
    - Therapeutic class: antiulcer agent
    - Pharmacologic class: proton pump inhibitor (PPI)
    - Schedule: not scheduled
* **NEVER, NEVER, NEVER GIVE A DRUG YOU ARE UNFAMILIAR WITH**
  + Make yourself very familiar with your Drug Handbook
  + Bring it to class

# Lecture 2 - 09/04/12 **MECHANISMS OF DRUG MOVEMENT**

**(Adam’s Ch. 4, 5 & 6)**

* **Pre-Questions**
  + **What is the difference between a generic and Trade name drug? How do you know which is which?**
    - The names of Trade name drugs are capitalized, whereas generics are not. There is only one generic name, but there can be several trade names. When a drug is originally approved, it is manufactured only under its original Trade name for a period of 17-y before the patent expires.
  + **What is the difference between OTC medications and prescription medications?**
    - OTC medications can be purchased without an exam or an Rx by a HCP; therefore, OTC meds are less expensive, but the correct drug may not be chosen for a person’s problem. Prescription medications require an exam and Rx by a HCP; therefore, a more informed decision is made as to medication, dose, and course length. However, this takes more time and money.
  + **Where should a nurse get information about medications?**
    - Pharmacists are big nurse allies. Also, we need to become very familiar with our drug handbooks. In addition, several online resources exist.
  + **What is a prototype drug?**
    - A well-studied representative of a class of drugs (i.e.: morphine is the prototype for opioid analgesics) to which all other drugs in that class are compared. This doesn’t necessarily mean it is superior to other drugs in its class.
  + **What is a controlled substance?**
    - A controlled substance is one that has potential for abuse; therefore, they are restricted by the FDA and DEA and require licensure and registration to dispense them. In the US, these are categorized from Schedule I-V from highest to lowest potential for abuse. Schedule V includes drugs with no therapeutic benefit such as heroin and marijuana (if so, why is marijuana prescribed??) and the highest risk for physical and psychological dependence; and Schedule I includes drugs that can be sold OTC such as hydrocodone as part of a combination drug.
* Objectives
  + Understand the role of pharmacokinetics and Pharmacodynamics in medication administration
  + Apply the principles of Pharmacotherapeutics to everyday nursing practice

## CH. 4 – Pharmacokinetics

* **Pharmacokinetics: How the Body Handles Medications** (4.1)
  + Roots:
    - Pharmaco – medicine
    - Kinetics – movement
  + Pharmacokinetics = the study of drug movement throughout the body
  + Understanding pharmacokinetics allows nurses to understand and predict the actions and side effects of medications
  + Medications are given to achieve a desirable effect; in order to accomplish this they must reach their target cells
    - A drug faces numerous obstacles in traveling to its target cell.
      * i.e.: crossing numerous plasma membranes, and being subjected to physiologic processes (such as digestion)
    - This is why dose level, bioavailability, and interactions are so important – a lot can go wrong along the way
  + 4 Phases (of pharmacokinetic processes) (Figure 4.1)
    - Absorption
    - Distribution
    - Metabolism
    - Excretion
* The Passage of Drugs Through Plasma Membranes (4.2)
  + 2 Main Processes Used:
    - Active Transport
      * Movement *against* concentration/electrochemical gradient
      * Includes cotransport
    - Diffusion/Passive Transport
      * Movement *along* concentration/electrochemical gradient
  + Given plasma membrane structure, some drugs have an easier time crossing plasma membranes than others
    - Large, hydrophilic, and/or charged molecules will not gain access without active transport
    - Small, hydrophobic, and/or nonpolar molecules can usually gain access through simple diffusion
  + Some drugs don’t pass through plasma membranes at all
    - Some act on membrane receptors (as ligands) to activate second-messengers (see 5.5)
* **Absorption of** **Medications** (4.3)
  + Movement of a medication from the site of its administration across body membranes to the circulatory system, where they become **systemic**
    - Drugs may be absorbed through the skin, mucous membranes, or the membranes that line the GI or respiratory tract in order to enter the circulatory system
      * Most drugs will be administered orally
      * When they reach the **liver**, the drug will be metabolized
  + Most drugs must be absorbed to have an effect
    - Some exceptions:
      * Topicals – work at skin level
      * Intestinal anti-infectives whose target is within the lumen of the intestines.
  + Absorption is the main determinant of the length of time it takes for a drug to produce its effect
    - The more rapid the absorption, the faster the onset of drug action
      * Therefore, rapidly absorbed drugs are key in critical care
    - Effect duration depends on drug half-life
  + Conditional on many factors:
    - Mode of administration
      * IV quickest (because they directly enter the circulatory system)
      * Liquids quicker than tablets
    - Blood flow to site of administration
    - Digestive motility
      * Diarrhea 🡪 drug moves fast through intestines, and has less time to be absorbed
    - Exposure to enzymes in the digestive tract
    - Surrounding pH
      * Acids absorbed better in acids; bases absorbed better in bases
        + Acids absorbed in the stomach
        + Bases absorbed in the small intestine
      * If drugs are ionized by their surrounding pH, their absorption is slow
        + Their absorption is slow because, as explained in 4.2, ionized molecules have a more difficult time passing through plasma membranes than nonionized
    - Drug-Drug interactions
      * i.e.: tetracycline + calcium 🡪 slower abx absorption
    - Drug food interactions
      * i.e.: high-fat food moves very slowly, and will therefore slow the movement of drugs taken with a meal
  + The nurse must be aware of these factors and must educate patients whenever necessary
* **Distribution of Medications** (4.4)
  + Involves the transport of medications throughout the body
  + Simplest determining factor is the amount of blood flow to the body tissue
    - Heart, liver, kidneys, and brain receive the most
    - Skin, bone, and adipose tissue receive less, therefore it is more difficult to get concentrated doses of medications to these areas
      * These areas also store medication (they have an especially high **affinity** for some meds)
  + Lipid-soluble agents are more completely and QUICKLY distributed than water-soluble agents
  + Many drugs bind to plasma proteins (particularly albumin) and form **drug-protein complexes**:
    - Too large to pass through capillary (plasma) membranes for distribution to body tissues
    - Accumulate in plasma until they are displaced by other protein-bound drugs or released from the complex
  + Only free (unbound) drug molecules can reach their target organs (move through plasma membranes), or be excreted by the kidneys
  + There are also anatomical barriers which inhibit many drugs and chemicals from entering
    - Blood-Brain Barrier
      * Drugs for brain cancer etc. must be able to cross this barrier – but most antitumor medications do not easily cross the blood-brain barrier, making brain cancer very hard to treat
    - Fetal-Placental Barrier
      * If drugs given to the mother can pass this barrier, it can cause devastating effects… Alcohol, cocaine, caffeine are a few examples of molecules that can pass the barrier
      * As a result, NO DRUG (herbal, OTC, or otherwise) should be taken by a pregnant patient without first checking its safety for the fetus
* **When giving multiple drugs that are highly protein-bound the nurse should monitor the patient closely for toxicity…why?**
  + i.e.: warfarin is 99% bound (only 1% is free to exert its effects) – if another drug is given that displaces warfarin (such as aspirin), more warfarin will be able to carry out effects…. the patient will bleed out!!!!!
* **Metabolism of Medications** (4.5)
  + Metabolism = Biotransformation
    - Process of chemically converting a drug to a form that is usually more easily removed from the body
  + Liver is the primary site
    - Drugs pass from stomach to liver via hepatic portal system
    - Drugs undergo many types of changes as they pass through the liver
      * Most by **hepatic microsomal enzyme system (the P-450 system)**
        + The primary function of the microsomal enzyme system is to inactivate drugs and accelerate their excretion

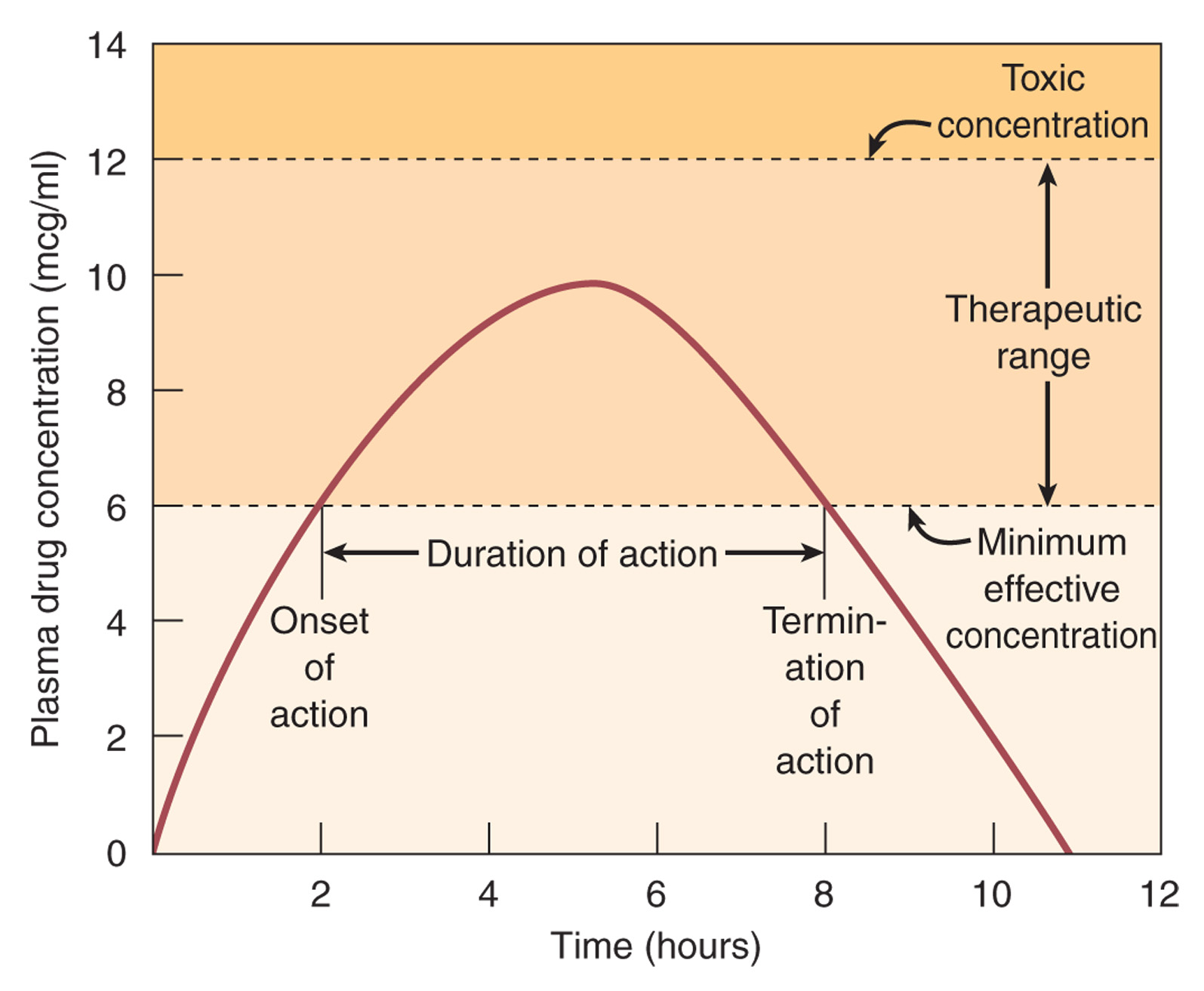
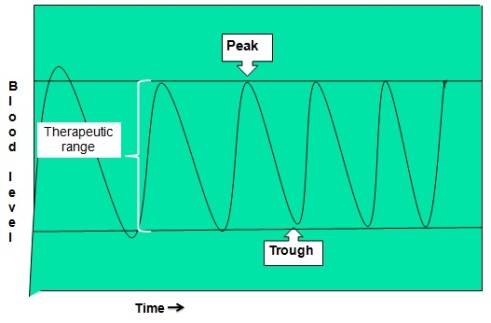
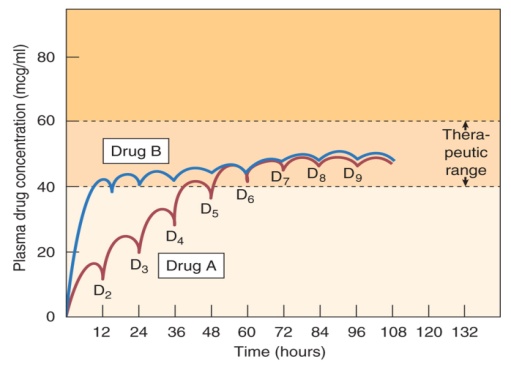
Some drugs cause **enzyme induction** – an increase in metabolic activity. This means that higher doses of medications may be required.

There are also a few drugs whose activity is INCREASED by enzymatic activity

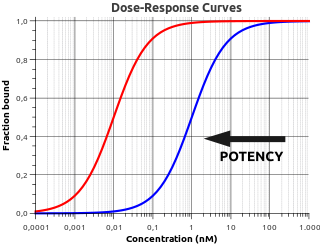
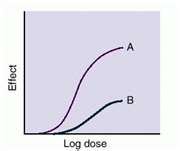
Some substances, called **prodrugs** are totally inactive until they are metabolized

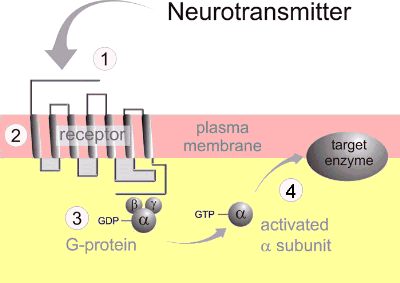
* + During drug metabolism, **conjugates** are added to molecules to increase their water solubility, facilitating excretion (by the kidneys)
  + Patients with decreased hepatic enzyme activity (lower hepatic metabolism) are more sensitive to drugs and need lower doses
    - Infants
    - Elderly
    - People with certain genetic disorders
    - Severe liver dz (cirrhosis)
      * THE NURSE MUST BE AWARE OF LAB VALUES WHICH INDICATE LIVER DZ SO DOSES CAN BE ADJUSTED
  + **First-Pass Effect**
    - **Drug absorbed and metabolized before it reaches the rest of the circulation**
      * All drugs which are absorbed after oral administration pass directly to the hepatic-portal circulation, which carries blood to the liver before it is distributed to other body tissues; therefore, some drugs may be **inactivated** by the liver before they reach **systemic circulation**.
    - Drugs that are rendered inactive by the first-pass effect must be given by another route:
      * Parenteral (IV)
      * Sublingual
      * Rectal (PR)
* **Excretion of Medications** (4.6)
  + Process by which drugs are removed from the body
  + The rate at which medications are excreted determines their concentration in the bloodstream/tissues
    - Concentration determines duration of action
  + Primary site of excretion is the kidney
    - Filters on average 180L of blood per day
    - Some drugs are small enough to be passively filtered at the glomerulus
    - Larger and/or protein-bound drugs have to be actively secreted into the distal tubule in order to be excreted
    - Urine pH also influences drug excretion
      * In patients who have overdosed on a medication (needs to be excreted ASAP) we can give another drug that changes urine pH in order to help the patient detox more quickly.
    - Kidney filtration mechanisms are less active in:
      * Infants
      * Elderly
      * Patients with Renal Dz
        + These patients retain drugs for an extended time
        + KIDNEY FUNCTION LAB VALUES AND DOSING REGIMES MUST BE FOLLOWED CLOSELY and OFTEN!!!
        + These patients are preferred to receive drugs that are eliminated through the feces

i.e. – biliary excretion

* + Drugs that change into gaseous forms can be excreted by the respiratory system
    - The better the patient’s gas exchange, the quicker the excretion.
  + Drugs can also undergo glandular excretion
    - Saliva, sweat, or breast milk
* **Drug Plasma Concentration and Therapeutic Response** (4.7)
  + Directly related to level in the plasma
    - The level of a drug at its target organ is impossible to measure (otherwise this would be a preferable measurement)
  + Minimum effective concentration
    - The amount of a drug required to produce a therapeutic effect
  + Toxic concentration
    - The level of drug that will result in serious adverse effects
  + Therapeutic range
    - The plasma drug concentration between minimum effective concentration and toxic concentration
    - The nurse’s goal is to keep a drug’s plasma concentration in the therapeutic range (don’t give ½ an aspirin for a bad headache… then again, don’t give 6!!!)
  + (See graph below!)
* **Effect of mode of administration on onset, peak, and duration of action**
  + In practice, nurses evaluate patient-drug response based on onset, peak, and duration of action
    - Vary for any drug depending on route of administration
      * PO – slower
      * IV – most rapid
      * IM – rapid
      * PR (per rectum) – variable
  + **In what situations might this information be especially helpful?**
    - Life-threatening, urgent problems that require resolution ASAP
* **Plasma Half-Life and Duration of Drug Action** (4.8)
  + Half-Life
    - See graph
    - Plasma half-life (t½) = the length of time required for the concentration of a drug to decrease by **½**
      * Conc. 10mcg/mL 🡪 5mcg/mL = **t½ = ~3h**
      * 2nd t½ will leave 2.5mcg/mL ( ½ of 5)
      * 3rd t½ will leave 1.25mcg/mL, etc. ( ½ of 2.5)
  + Plasma t½ determines how often a drug must be administered to maintain therapeutic level
    - Shorter plasma half-life (more often)
    - Longer plasma half-life (less often)
  + IF A PATIENT HAS SEVERE RENAL OR HEPATIC DZ THE PLASMA HALF-LIFE WILL INCREASE AND DRUGS WILL NEED TO BE GIVEN LESS FREQUENTLY TO AVOID TOXICITY!!!
* **Therapeutic Level**
  + To reach a therapeutic level of a drug in the bloodstream several doses must be given
    - It takes approximately 4 half-lives (4 doses)
  + At the therapeutic level the amount administered has reached the amount of drug being eliminated
    - This results in the distribution of a continuous therapeutic level of drug to body tissues
* **Peak and Trough Drug Levels**
  + Peak
    - Drawn at time of highest level after administration
  + Trough
    - Drawn just prior to next dose
  + Used to monitor levels to maintain them in optimal range, avoiding toxic or sub-therapeutic levels
* **Loading Doses and Maintenance Doses** (4.9)
  + Few drugs are given as a single dose… repeated dosing results in an accumulation of drug in the bloodstream until it plateaus within therapeutic range
    - It plateaus because the amount of drug being administered and the amount of drug being excreted have reached equilibrium.
  + The therapeutic level may be reached faster by administering a **loading dose**
    - A loading dose is a higher dose of drug that is given once or twice to prime the bloodstream with a level sufficient to quickly induce a therapeutic response
    - i.e.: prednisone taper
  + Before the plasma level can drop back to zero, **maintenance doses** are given to keep the plasma drug concentration in the therapeutic range
  + In the Figure (5.7) Drug B reaches therapeutic level faster than drug A because a loading dose was given
  + Loading doses are unnecessary when drugs are given by continuous IV infusions – through this method, the plateau is reached quickly and there are few (if any) fluctuations in drug plasma levels

## CH. 5 – Pharmacodynamics

* **Pharmacodynamics and Interpatient Variability** (5.1)
  + Roots:
    - Pharmaco – medicine
    - Dynamics – change
  + Pharmacodynamics = the study of how drugs change the body
    - More completely – it is a branch of pharmacology concerned with the mechanisms of drug action and the relationships between drug concentration and responses in the body
  + All body functions occur at the cellular level. Drugs are chemicals that alter basic processes in body cells
    - They **stimulate** or **inhibit** normal cellular functions
      * i.e.: Agonist vs. antagonist
    - The cannot create functions or activities
  + **The goal of drug therapy is to choose optimal doses to produce the desired effect in a patient while avoiding adverse effects**
    - There is a wide variation in optimal doses among patients (due to Interpatient variability)
    - The **median effective dose** (ED50) is the dose required to produce a specific therapeutic response in 50% of a group of patients
  + The nurse must observe the patient, take vital signs, and look at lab data to determine if the standard dose is right for this particular patient.
    - * Adjustments are key to producing the desired response (think of a patient with renal disease, for example)
  + Factors effecting patient-drug response
    - Dosage
    - Route of administration
      * IV faster than IM
    - Drug-diet interactions
    - Drug-Drug interactions
    - Age
    - Body weight
      * & BMI – influence of fat on absorption
    - Ethnicity
    - Gender
    - Pathologic conditions
      * Renal/Hepatic dz.
    - Tolerance
      * More tolerance means that you need more medicine to maintain therapeutic effects
* **Therapeutic Index and Drug Safety** (5.2)
  + Median lethal dose (LD50)
    - Determined in preclinical trials and is the dose that will be lethal in 50% of lab animals
  + Therapeutic Index
    - The relationship of a drug’s median effective dose to its median lethal dose
    - Therapeutic Index = LD50/ED50 🡪 50mg/10mg = **5**
    - The higher the Therapeutic Index, the safer the medication
  + Median toxic dose (TD50)
    - Extrapolated from animal data or based on adverse effects recorded in patient clinical trials
* **The Graded Dose-Response Relationship and Therapeutic Response** (5.3)
  + Graded Dose-Response Relationship
    - Measures of an individual patient’s response to a drug at different doses.
      * Graphic is called a dose-response curve
        + Phase 1 – lowest doses – few target cells effected
        + Phase 2 - most desirable range – more drug produces more therapeutic effect
        + Phase 3 – therapeutic plateau – more drug has no additional therapeutic effect
    - Some patients will have a therapeutic effect at a lower dose
* **Potency and Efficacy** (5.4)
  + Within a pharmacological class not all drugs are equally effective; there are two ways to compare drugs within the same class
    - Potency
      * A drug that is more potent will produce a therapeutic effect at a lower dose
        + Therefore, in the graph, the Red Drug is more potent than the Blue Drug because the same effect is achieved with lower concentration.
    - Efficacy
      * The magnitude of maximal response that can be produced from a drug corresponds to its efficacy
      * i.e.: Morphine has higher efficacy than aspirin for severe pain
      * To have the same impact
        + Therefore, in the graph, A would be morphine and B would be aspirin (effect is greater, even though dose is lower)
      * From a pharmacotherapeutic standpoint, efficacy is more important than potency – it’s the ability to relieve symptoms that prevails as the more important factor (that said, if two drugs are equivalent in efficacy, it is likely better to use the more potent one – which produces the same effect but with a smaller dose)
* **Cellular Receptors and Drug Action** (5.5)
  + Drugs act by changing existing physiologic and biochemical processes, they cannot create processes
    - Drugs bind to **receptors** whose normal function is to bind to endogenous (naturally occurring) molecules such as hormones, neurotransmitters, and growth factors
      * Drugs then act as agonists or antagonists to the functions of their target cells
      * This theory explains the mechanism by which most drugs produce their effects
  + A drug attaches to its receptor like a lock and key
    - Small changes to the structure of a drug or its receptor may weaken or eliminate binding
    - Binding either initiates or inhibits normal activity of the cell:

****

* + - * Image: a ligand (in this case, a neurotransmitter) binds to a G-protein receptor. A drug whose target is this receptor could replace the neurotransmitter in binding to this site, and could then activate (agonistic action) or inhibit (antagonistic action) the function normally performed by the neurotransmitter. In this case, the action of the neurotransmitter is to activate a target enzyme, so the drug could either help this process (activate the G-protein) or just block the neurotransmitter from performing this function.
  + Receptors can be on the plasma membrane, or within the cell
    - If a drug can get past the plasma membrane, only then can it can access an intracellular receptor
  + Receptor sub-types are being discovered and new medications are being developed; *the more specific the receptor, the fewer the side-effects*
  + Drugs can also act independently of cellular receptors by:
    - Altering membrane permeability (allowing more or less substances to enter target cells)
    - Depressing membrane excitability (inhibitory effect)

Altering activity of cellular pumps

* **Types of Drug-Receptor Interactions** (5.6)
  + Types of Drug-Receptor Interactions:
    - Agonist
      * Drug that produces the same type of response as the endogenous substance
    - Partial agonist
      * Produces a weaker response than an agonist
    - Antagonist
      * Drug that occupies a receptor and prevents the endogenous substance (or another drug) from acting
      * *Functional* antagonism inhibits the effects of an agonist by changing pharmacokinetic factors (i.e. – speeding up metabolism so another drug is eliminated from the body)
  + Relationships between agonists and antagonists explains many drug-drug and drug-food interactions
* **Pharmacology of the Future: Customizing Drug Therapy** (5.7)
  + Pharmacogenetics
    - Due to lack of response or adverse effects, there may currently be limited effectiveness of currently available drugs
      * Inadequate addressing of “idiosyncratic responses” due to limited drug specificity and Interpatient variability
    - In the future, pharmacologic treatment based on DNA evaluation will play a progressively larger role
      * Drug customization based on genetic similarities
* **PRACTICE**
  + **Morphine**
    - Action: binds to opiate receptors in CNS. Alters the perception of and response to painful stimuli while producing generalized CNS depression
  + **Motrin** (ibuprofen)
    - Action: Inhibits prostaglandin synthesis
      * + (prostaglandin – paracrines whose function includes regulating the contraction and relaxation of smooth muscle – this explains why ibuprofen is so effective at treating dysmenorrhea)
  + **Cardizem** (diltiazem) (assume PO administration)
    - Onset: 30 minutes
    - Peak: 2-3 hours
    - Duration of action: 6-8 hours
    - Action: inhibits transport of calcium into myocardial and vascular smooth muscle cells, resulting in inhibition of excitation-contraction coupling and subsequent contraction (ergo, vasodilation)
    - Other:
      * may increase digoxin levels
      * grapefruit juice increases its levels and effect
  + **metformin** (assume PO administration)
    - Onset: unknown
    - Peak: unknown
    - Duration of action: 12 hours
    - Action: decreases hepatic glucose production, decreases intestinal glucose absorption, increases sensitivity to insulin
  + **Digoxin** (assume PO administration)
    - Onset: 30-120 minutes
    - Peak: 2-8 hours
    - Duration of action: 2-4 days
    - Action: increased the force of myocardial contraction, prolongs refractory period of the AV node, decreases conduction through the SA and AV nodes

## CH. 6 – The Nursing Process in Pharmacology

* **Pre-Questions**
  + **What are the 4 processes involved in Pharmokinetics?**
    - Absorption, Distribution, Metabolism, and Excretion
  + **What is the significance of a drug which is protein-bound?**
    - A protein-bound drug is only exerting a certain percentage of its effect (for example, warfarin is 99% bound, so only 1% of the drug is active). This is important to know because drug interactions can alter how much of a drug is bound.
  + **What are some of the potential problems with drugs that are protein-bound?**
    - If a drug that is largely protein-bound is displaced (by another drug) the patient may experience toxicity
    - If a patient has poor nutritional status (low blood albumin) then there are fewer plasma proteins for a drug to bind to – which can also cause toxicity
  + **What is the first-pass effect?**
    - When a drug is metabolized and inactivated before it reaches systemic circulation. This occurs when a drug is administered orally, causing the drug to be absorbed first into hepatic portal circulation.
  + **How do we alter administration of a drug that is affected by the first-pass effect?**
    - Alternative routes of administration (IV, PR, sublingual)
  + **What is an agonist?**
    - A drug that increases the effect of the target receptor’s endogenous molecule
  + **What is an antagonist?**
    - A drug that decreases the effect of the target receptor’s endogenous molecule
  + **What effect would an antacid have on a drug?**
    - An antacid would create a less acidic environment in the patient’s stomach. If the drug were an acid, it would need to be absorbed in an acidic environment, so the antacid would antagonize the effects of the drug.
  + **What is the definition of half-life?**
    - The amount of time it takes for the plasma concentration of a drug to reduce by ½
  + **What is peak and trough?**
    - The high- and low-end limits of the therapeutic range, respectively.
  + **What is the therapeutic index? How is it determined?**
    - The therapeutic index is a measure of drug safety. It is determined by dividing the median lethal dose by the median effective dose. The larger the resulting number, the safer the drug.
* **Medication Knowledge and the responsibilities of the nurse**
  + The Five (*Six*) Rights of Drug Administration
    - Right Patient
    - Right Medication
    - Right Dose
    - Right Route
    - Right Time
    - *Right Documentation*
  + The nurse is responsible to know:
    - What drug is ordered
    - Name
      * Generic and trade
    - Classification
      * Therapeutic/Pharmacological
    - Intended or proposed use (ACTION)
    - Effects on the body
    - Contraindications
    - Special considerations
      * i.e.: how age, weight, body fat distribution, and individual pathophysiological states affect response
    - Side-Effects
  + Other knowledge:
    - Why the medication was prescribed for this particular patient
    - How the medication is supplied by the pharmacy
    - How the medication is to be administered, including dosage ranges
    - What nursing process considerations related to the medication apply to this patient
* **ALLERGIES**
  + **EVERY TIME YOU ADMINISTER A MEDICATION YOU MUST ASK A PATIENT IF HE HAS ANY ALLERGIES**
  + Allergic reaction:
    - An acquired systemic hyperresponse of body defenses to a foreign substance
    - Signs and symptoms vary in severity, and include:
      * Rash
      * Itching
      * Edema
  + Anaphylaxis:
    - A severe type of allergic reaction that involves massive systemic release of histamine and can lead to life-threatening shock
    - Characterized by hypotension, difficulty breathing, changes in heart rate
* **The Nursing Process in Pharmacology**
  + The nursing process is essential to pharmacology
  + It is a systematic method of problem-solving
  + Forms the foundation of all nursing practice
  + Is essentially five steps:
    - Assessment
    - Diagnosis
    - Planning
    - Implementation
    - Evaluation
* **Assessment of the Patient** (6.1)
  + The systematic collection, organization, validation, and documentation of patient data
  + Begins with the nurse’s initial contact with the patient and continues with every contact
  + Gathering of baseline data
    - Subjective
      * “I have a 9 out of 10 headache.”
      * Take what the patient is saying seriously
    - Objective
      * Physical assessment
      * Vital Signs
      * Height
      * Weight
      * Laboratory Values
        + Hepatic/Renal/Electrolyte Values all very important
  + Health History (tailored to the patient’s clinical condition) (Table 6.1)
    - Chief Complaint
    - Allergies
    - Past medical History
    - Family History
    - Medication history/OTC/herbal
    - Health management
    - Reproductive history
    - Personal-social history (alcohol/tobacco/caffeine)
      * Alcohol intake is important to know, as it may affect medications
    - Health risk history
  + What is *not* being said may be as important as what *is* being said
  + The effectiveness of drug therapy must be evaluated
    - If drugs aren’t providing desired therapeutic effects, more assessment is necessary to determine why
    - Any adverse effects must also be assessed (including follow-up vitals and labs)
  + **An assessment of the ability of the patient to assume responsibility for self-administration of medications is necessary**
    - Make sure the patient knows how to take his medications – have him repeat it back to you, preferably at multiple occasions
  + Factors which have to be evaluated are the patient’s:
    - Financial ability to afford Rx
    - Physical ability to dispense (open bottles, etc.)
    - Ability to understand dosing and intended effect
    - Ability to contend with:
      * Intended effects
      * Side effects
* Medication Errors and Dietary Supplements
  + Patients should be encouraged to report use of all OTC dietary supplements
  + The HCP should NOT underestimate the effects of dietary supplements – they can act as agonist or antagonists to Rx medications
    - i.e. – garlic + warfarin 🡪 abnormal bleeding!
* **Nursing Diagnoses** (6.2)
  + Once the baseline data has been gathered, a Nursing Diagnosis is made
  + NANDA definition:
    - A clinical judgment about individual, family, or community responses to actual or potential health/life processes. Per NANDA, Nursing Diagnoses provide the basis for selection of nursing interventions to achieve outcomes for which the nurse is accountable
    - In other words:
      * Nursing diagnosis focuses on a patient’s response to a health or life process, and are used as the basis for establishing goals and outcomes
        + Goals: what the patient will be able to achieve
        + Outcomes: objective measurement of these goals

Goals and Outcomes must be prioritized based on assessment data and nursing diagnoses: i.e. – relief of pain is a priority over nausea

* + Example:
    - While assessing a patient, he asks you questions which indicate his lack of understanding about the importance of his medication
      * Nursing Diagnosis: **Knowledge Deficit** related to drug therapy (Table 6.2 has more diagnoses)
      * Goal: for the patient to demonstrate an understanding of the drug’s action
      * Outcome: the patient accurately describing the drug’s action and side-effects
  + In terms of pharmacotherapy, the diagnosis phase of the nursing process addresses these main areas:
    - Promoting therapeutic drug effects
    - Minimizing adverse drug effects and toxicity
    - Maximizing the ability of the patient for self-care, including the knowledge, skills, and resources necessary for safe and effective drug administration
* **Planning: Establishing Goals and Outcomes** (6.3)
  + Care Plans
    - Once the Nursing Diagnosis has been made and the goals and outcomes determined, a Nursing Care Plan is formulated
    - The Care Plan describes the steps that will be followed to reach the desired goals and outcomes
    - In terms of pharmacotherapy, the planning phase of the nursing process involves 2 main components:
      * Drug administration
    - Patient Teaching
  + **Hint: Use Nursing Process Focus and Nursing Dx in the textbook** (end of each chapter)
    - * They will guide us to what is important and unique about the drugs used, and will help formulate patient teaching
* **Implementing Specific Nursing Actions** (6.4)
  + Putting the plan into *action*
    - i.e.: administering a drug; teaching the patient about the drug and its side-effects, etc.
  + This phase also includes monitoring the effects of the teaching, and of the drug itself
    - Both effectiveness, and adverse effects
    - A thorough knowledge of the actions of each medication is necessary to carry out this monitoring process.
  + Teaching is a primary role for nurses
    - JCAHO gives it weight in law… it is of key importance in accreditation standards
    - Every nurse-patient interaction can present an opportunity for teaching, which should be taken advantage of because smaller portions of education over time are more effective than cramming it all into one session.
    - See Table 6.3
  + Note on Pediatrics
    - Be sure to note differences in dosing from adult standards – small errors can have serious consequences
* **Evaluating the Effects of Medications** (6.5)
  + Evaluates the effectiveness of the implementation of the Care Plan
    - Compares current status with desired outcome
  + The process comes full circle, as the nurse reassesses the patient, and changes the goals and outcomes accordingly
  + Evaluation is not the end of the cycle, but the beginning of the next cycle
    - Partially met goals require continued interventions
      * i.e. – increasing the drug dose to achieve therapeutic levels
* **Areas of Patient Teaching on Medications**
  + Therapeutic use and outcomes
  + Monitoring side effects and adverse effects
  + Medication administration
  + Other monitoring and special requirements